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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/096,749	06/12/98	KOIDE	S 109.034US1

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HM22/0122

EXAMINER	
HELMS, L	
ART UNIT	PAPER NUMBER
1642	15

DATE MAILED: 01/22/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/096,749	Kolde et al
Examiner	**Group Art Unit**
Larry R. Helms Ph.D.	1642

☒ Responsive to communication(s) filed on *27 Nov 2000*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-6* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-6* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 7-39 have ben canceled.

Claims 1-6 have been amended.

Claims 1-6 are under examination.

2. The text of those sections of title 35, USC Code not included on the Office Action can be found in a prior Office Action.

3. The following Office Action contains some NEW GROUNDS of rejection.

Information Disclosure Statement

4. The IDS filed 11/27/00 as paper # 12 has been considered, however, the reference of Holm et al, Science 273:595-60, has not been considered because the reference was not provided.

Rejections Withdrawn

5. The rejection of claims 1-6 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

6. Claims 1-6 are rejected under 35 U.S.C. 102(a or b) as being anticipated by Koide et al (IDS # 5) is withdrawn in view of the declaration of Anne Koch.

Response to Arguments

7. The rejection of claims 1-6 under 35 U.S.C. 112, first paragraph is maintained.

The response filed 11/27/00 has been carefully considered but is deemed not to be persuasive. The response cites several references as evidence that the many mutations in the beta-strand domain of FN3 have a minor effect on the activity and thus one can engineer mutant FN3 that retains the binding function by introducing mutations in the beta-strand domain (see pages 8-9 of response). In response to this argument, the references cited that provide evidence that FN3 is one of the most extensively studied protein domains is not related to the enablement rejection. The rejection did not conclude that FN3 does not have the structure of a beta-strand domain. In regards to the reference of Cota et al, the reference is directed to the Fnfn10 and Tnfn3 domains and Cota et al teach that the two proteins have 62% sequence similarity but do not have the same stability or the same result to mutations. Claim 1 recites that the beta-strand domain of the monobody has at least 50% total amino acid sequence homology to the wild type Fn3 domain, as such the TnFn3 domain would be encompassed by the claim and thus, as evidenced by Cota et al would not be stable to all mutations. In addition Cota states "This study emphasises the difficulties that might arise when making generalizations from a single member of a protein family" (see abstract).

The response continues with a declaration by Dr. Koide. The declaration of Dr. Koide has been carefully considered but is deemed not to be persuasive. The declaration discusses insertions of glycine residues in BC, DE, and FG loops. The result of the insertions were as stated destabilizing but highly stable. The data is provided for the entire FN3 domain and the

results are not commensurate in scope with the claims because the claims are directed to (1) at least two Fn3 beta-strand domains which would not be as stable as the entire Fn3 domain and the specification does not teach any successful insertions in only two beta-strand domains, and (2) the claims encompass deletions, insertions or replacements of 2 to 25 amino acid residues in any loop and the specification fails to teach deletion of up to 25 amino acids in a loop. In addition, the response does not address the unpredictability in the art as evidenced by Helms et al for insertions of amino acids in loops. Moreover, the response does not address the lack of enablement for any loop region that catalyzes a chemical reaction such that the ratio of kcat/kuncat is greater that 10. Therefore, one skilled in the art would be forced into undue experimentation in order to practice the broadly claimed invention.

8. The rejection of claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Main et al (Cell 71:671-678, 1992, IDS #5 and further in view of Lee et al (Protein Engineering 6:745-754, 1993, IDS # 8) is maintained.

The response filed 11/27/00 has been carefully considered but is deemed not to be persuasive. The response states that "Main et al do not teach or suggest that one could engineer binding molecules by altering loop sequences of the Fn3 scaffold" (see page 12 of response). In addition, the response states "Lee et al teach away from the present solution" see page 12 of response). In response to these arguments, Lee et al does not teach away as the response states. The reference of Lee et al must be taken in its entirety and not just for one statement that was in

the introduction and taken out of context. The cited part of Lee et al describes the art prior to the work of Lee et al and Lee et al clearly demonstrates that a presentation molecule can display an installed peptide sequence that allows receptor binding, while at the same time provides sufficient structural interactions to constrain conformation (this rebuts response on page 12 bottom of page). Main et al teach that the Fn3 topology is similar to immunoglobulins and functional loops can be built onto a structural framework. Thus, the fact remains that it would have been obvious to one of ordinary skill in the art to use the Fn3 domain of Main et al, which has a fold similar to the immunoglobulin of Lee et al, and replace residues in the surface exposed loops with residues that would bind to a binding partner as taught by Lee et al.

The following is a NEW GROUND of rejection.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 has been amended to recite "at least two Fn3 β-strand domain sequences" and "two to 25 amino acids" and claim 5 has been amended to recite "2 to 25 amino acids". The response filed 11/27/00 is silent as to where support for the limitations are. This is not sufficient because support needs to be provided by the specification as originally filed. Applicant is required to either point to where the specification provides support for the phrase or to remove it from the claims.

Conclusions

11. No Claims are allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Respectfully,

Sheela J. Huff
SHEELA HUFF
PRIMARY EXAMINER

Larry R. Helms Ph.D.

703-306-5879